General

Guideline Title

ACR Appropriateness Criteria® prostate cancer—pretreatment detection, staging and surveillance.

Bibliographic Source(s)

Eberhardt SC, Carter S, Casalino DD, Merrick G, Frank SJ, Gottschalk AR, Leyendecker JR, Nguyen PL, Oto A, Porter C, Remer EM, Rosenthal SA, Expert Panels on Urologic Imaging and Radiation Oncology-Prostate. ACR Appropriateness CriteriaÂ® prostate cancer -- pretreatment detection, staging, and surveillance. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 12 p. [119 references]

Guideline Status

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

Recommendations

Major Recommendations

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary. The recommendations that follow are based on the previous version of the guideline.

ACR Appropriateness Criteria®

Clinical Condition: Prostate Cancer — Pretreatment Detection, Staging, and Surveillance

Variant 1: Prostate cancer diagnosed on biopsy, patient at low risk for locally advanced disease and metastases (AJCC Group I). Example: PSA ≤10 and Gleason ≤6 and clinical stage T1 or T2a.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	5	May be appropriate for active surveillance. See statement regarding contrast in text under "Anticipated Exceptions."	O
MRI pelvis without contrast	4	May be appropriate for active surveillance.	O
CT abdomen and pelvis with contrast	2		☢☢☢☢
CT abdomen and pelvis without contrast	2		☢☢☢☢
Tc-99m bone scan whole body	2		☢☢☢

Radiologic Procedure	Rating	Comments	RRL*
X-ray area of interest	2		Varies
FDG-PET/CT whole body	2		☢☢☢☢
CT abdomen and pelvis without and with contrast	1		☢☢☢☢
In-111 capromab pendetide scan	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Prostate cancer diagnosed on biopsy, patient at intermediate risk for locally advanced disease and metastases (AJCC Groups IIA or IIB). Example: PSA 10-20 or Gleason 7 or clinical stage T2b.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	7	Should include dynamic contrast-enhanced (DCE) technique. See statement regarding contrast in text under "Anticipated Exceptions."	O
MRI pelvis without contrast	6		O
CT abdomen and pelvis with contrast	6		☢☢☢☢
Tc-99m bone scan whole body	5		☢☢☢
CT abdomen and pelvis without contrast	4	If contrast contraindicated.	☢☢☢☢
X-ray area of interest	4	Appropriate if bone scan or symptoms suggest possible involvement.	Varies
CT abdomen and pelvis without and with contrast	2		☢☢☢☢
In-111 capromab pendetide scan	2		☢☢☢☢
FDG-PET/CT whole body	2		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Prostate cancer diagnosed on biopsy, patient at high risk for locally advanced disease and metastases (AJCC Groups III and IV). Example: PSA ≥20 or Gleason 8-10 or clinical stage T2c or higher.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	8	Should include dynamic contrast-enhanced (DCE) technique. See statement regarding contrast in text under "Anticipated Exceptions."	O
Tc-99m bone scan whole body	8		☢☢☢
CT abdomen and pelvis with contrast	7		☢☢☢☢
MRI pelvis without contrast	6		O
CT abdomen and pelvis without contrast	6	If contrast contraindicated.	☢☢☢☢
X-ray area of interest	4	Appropriate if bone scan or symptoms suggest possible involvement.	Varies
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative**

Radiologic Procedure	Rating	Comments	RRL*
FDG-PET/CT whole body	4		☢☢☢☢
CT abdomen and pelvis without and with contrast	2		☢☢☢☢
In-111 capromab pendetide scan	2		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 4: Multiple negative prostate biopsies, but there is concern for prostate cancer based upon rising or persistently elevated serum markers suggestive of cancer.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	7	Should include dynamic contrast-enhanced (DCE) technique. See statement regarding contrast in text under "Anticipated Exceptions."	O
MRI pelvis without contrast	5		O
CT abdomen and pelvis with contrast	2		☢☢☢☢
CT abdomen and pelvis without contrast	2		☢☢☢☢
CT abdomen and pelvis without and with contrast	2		☢☢☢☢
In-111 capromab pendetide scan	2		☢☢☢☢
Tc-99m bone scan whole body	2		☢☢☢
X-ray area of interest	2		Varies
FDG-PET/CT whole body	2		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Prostate cancer is the most common noncutaneous malignancy of men in the United States and is the second leading cause of cancer mortality in American men, accounting for an estimated 28,170 deaths in 2012. Recommendations regarding serum prostate-specific antigen (PSA) screening and digital rectal examination (DRE) have been in flux. The American Urological Association (AUA) has lowered the age recommendation for obtaining baseline PSA to 40 years and no longer recommends a single threshold value of PSA to prompt biopsy. It now indicates that multiple factors should be taken into account, including DRE, PSA subsets, patient age, family history and ethnicity. The AUA and American Cancer Society now emphasize that risks of testing, such as overdetection and overtreatment, should be discussed with patients along with its benefits. Similarly, the latest early detection guidelines from the National Comprehensive Cancer Network expressed similar concerns. The authors did not reach consensus on this issue, but the majority recommended offering baseline PSA assessments at age 40, after discussion with patients of the risks and benefits of early detection.

Prostate Cancer Diagnosis

If either the DRE or PSA test suggests malignancy, a transrectal ultrasound-guided needle biopsy of the prostate gland is usually performed. However, in instances when a patient has a negative biopsy (generally more than one biopsy session), but there is a high clinical suspicion based on increased PSA or persistently elevated PSA, imaging with magnetic resonance imaging (MRI) can be used to detect prostate cancer, and guided biopsies can then be performed.

Pretreatment staging is important, because clinically localized disease (stage T1 or T2) is generally amenable to local therapy, while more advanced disease may require multimodal therapy (e.g., androgen deprivation therapy and radiation therapy). The staging system developed by the American Joint Committee on Cancer (AJCC) is used for pretreatment clinical staging and encompasses the status of the primary tumor (T), the lymph nodes (N), and any metastasis (M) (see Appendix 1 in the original guideline document).

Clinical Staging Methods Not Involving Imaging

Physical Examination

The DRE is considered insensitive for detecting extracapsular tumor extension. At least 40% of patients with cancers judged to be clinically confined (T1 or T2) by DRE are found to have extraprostatic extension at surgery. Thus, DRE alone has proven unsatisfactory for determining stage.

Prostate-specific Antigen

Serum PSA has been used as a screening serum biomarker to determine whether prostate biopsy is needed. PSA is also incorporated into predictive models for staging, especially when combined with the results of DRE and the biopsy Gleason score. PSA is also utilized in monitoring treatment response. In general, the higher the PSA, the more advanced the disease; moreover, the likelihood of having organ-confined disease is inversely proportional to the level of the PSA. Despite its utility, it is clear that as many as 15% of men with a normal PSA will have prostate cancer on one or more biopsy cores. Data also suggest that the correlation with extent of disease is poor for men with relatively low PSA levels (e.g., <9 ng/ml). In addition, use of PSA as a screening tool leads to increased prostate cancer diagnosis but appears to have little if any impact on cancer-specific mortality.

The initial PSA value correlates with the likelihood of being free of biochemical evidence of persistent disease and surviving prostate cancer. PSA measurements are evaluated alone or by comparison with a prior measurement (PSA velocity and PSA doubling time [PSADT]), or in the context of the patient's gland volume (PSA density). There are also age-specific PSA levels available. The density and age specificity help to separate the elevations in PSA due to benign prostatic hyperplasia (BPH) from those due to cancer; however, these methods provide guidance only on the likelihood of cancer versus benign disease. The use of PSA level alone to predict final pathologic stage in an individual has a prohibitively high false-positive rate. PSA as it has been discussed thus far can be more accurately termed total PSA (tPSA), since the bound and free components of PSA can be measured. Free PSA (fPSA) (i.e., not bound to plasma proteins) is relatively lower in patients with cancer than in those with BPH. As an example, fPSA fraction <15% has been associated with more aggressive tumors, whereas an fPSA fraction >25% generally indicates the presence of low-risk tumors.

Biopsy Results

The Gleason histologic grading system has been shown to correlate well with the extent of disease and prognosis. It is the single best predictor of the biological activity, and therefore the stage of the tumor. Gleason grade ranges from 2 (well differentiated, minimally aggressive) to 5 (anaplastic, highly aggressive). The Gleason score sum is based on the addition of major and minor histologic patterns. Thus a biopsy specimen with dominant grade 4 and minor grade 3 would get Gleason score 7. The probability of seminal vesicle invasion and lymph node involvement (SVI, LN+) increases with the Gleason score, and investigators have found a combination of the Gleason score and the serum PSA level to give the greatest prognostic information. Biopsy regimens are known to yield some falsely negative findings and to undersample some significant cancers. About 25% of patients who have Gleason score 6 based on the findings of biopsies guided by transrectal ultrasound (TRUS) will be found to have more aggressive disease after radical prostatectomy. MRI guidance for biopsies has shown improvement in diagnosing clinically significant cancers relative to TRUS guided biopsies. In a recent series, 41% of men with prior negative TRUS biopsy but suspected of having prostate cancer were diagnosed with prostate cancer with MRI guided biopsy.

Nomograms and Risk Group Stratification

Work by several groups of investigators has led to the development of nomograms that predict the probability of extracapsular extension (ECE), SVI, and LN+. These predictive models have been validated and led to attempts to correlate nomograms with prognosis. Most nomograms use combinations of clinically available data such as PSA level, Gleason score, and physical examination T stage to stratify the patient to a category of risk for locally advanced and metastatic disease. Clinicians have widely adopted a simplified approach to predicting outcome based on the same pretreatment parameters used in the nomograms. Using such an approach, patients with similar risk of biochemical recurrence can be divided into risk groups that, with additional follow-up, have been correlated with mortality:

- Low risk: AJCC clinical stage T1c or T2a and PSA ≤10 ng/mL and biopsy Gleason score ≤6: ~80% 10-year PSA failure-free survival rate.
- Intermediate risk: AJCC clinical stage T2b or PSA >10 and ≤20 ng/mL or biopsy Gleason score 7: ~50% 10-year PSA failure-free

survival rate.

- High risk: AJCC stage T2c disease or PSA >20 ng/mL or biopsy Gleason score ≥8: ~33% 10-year PSA failure-free survival rate.

Alternative risk stratification schemes have also been described, and despite their differences they support the notion that Gleason score, DRE T stage, and PSA can be used to predict survival and direct therapy. Some authors have found that the number of positive biopsies (e.g., >3) and the percentage of each core that is positive at biopsy (e.g., >50%) have been associated with increased risk of recurrent disease. However, some authors have found that the addition of the percentage of positive cores to existing models has had only minimal incremental benefit.

Summary of Nonimaging Methods of Staging

While DRE, PSA, or Gleason score individually predict stage, they are less accurate than when they are combined into nomograms that provide estimates of risk for locally advanced and metastatic disease. Imaging potentially improves these general estimates of risk by specifically identifying lesions with anatomic abnormalities. However, imaging findings should be interpreted in the context of the nonimaging findings. Due in part to the limitations of clinical staging, efforts have been made to use imaging modalities to better predict the extent of disease and outcome.

Imaging Methods

Ultrasound

Gray-scale ultrasound (US) has not proven satisfactory for local staging of prostate cancer. The ability of TRUS to predict ECE varies widely from 37% to 83% in different settings and populations; however, it is generally acknowledged that US is of limited value due to limitations of its spatial resolution. The addition of color Doppler and power Doppler has been reported to improve the detection of prostate cancer by identifying increased vascularity but has not yet been shown to improve staging accuracy. Contrast-enhanced US has the potential to substantially improve the staging of prostate cancer but has not yet been tested in a multi-institutional trial. Similarly, three-dimensional (3D) US is under investigation to improve the delineation of the cancer and prostate capsule.

Magnetic Resonance Imaging

Prostate imaging with MRI can be performed without or with endorectal coil. Endorectal coil magnetic resonance imaging (erMRI). Whether at 1.5T or higher field strength, provides the highest spatial resolution among the imaging modalities currently available. In conjunction with larger-field-of-view T1-weighted and T2-weighted sequences of the pelvis to assess for pelvic adenopathy and bone metastases, four MRI methods have been used to image and stage prostate cancer locally: high resolution T2- weighted MRI, MR spectroscopic imaging (MRSI), diffusion weighted MRI (DWI-MRI), and dynamic contrast-enhanced MRI (DCE-MRI). It is generally accepted for 1.5T imaging that an endorectal coil is required to achieve sufficient signal-to-noise ratios to allow small-field-of-view (12-16 cm) imaging which, in turn, allows images to be acquired with high resolution (~0.5 mm). Additionally, 3-Tesla (3T) erMRI may be beneficial by providing higher signal, thus further improving spatial (or temporal, in the case of DCE-MRI) resolution. One group of researchers has shown that 3T erMRI imaging is accurate for staging of prostate cancer, with moderate to substantial interobserver agreement, and that minimal capsular invasion could be detected. However, there are insufficient data in the literature to support definitive superiority of 3T erMRI over 1.5T. Staging using MRI with endorectal coil at 1.5T has been found superior to 3T without endorectal coil; however, more reports on 3T accuracy without endorectal coil are needed to properly judge its efficacy.

T2-weighted Magnetic Resonance Imaging

Over 20 years of clinical experience exists with T2-weighted erMRI. Technical improvements in MRI have led to excellent image quality and resolution, but there are intrinsic complexities in imaging prostate cancer that limit staging accuracy. Low-signal lesions on T2-weighted imaging can be due to cancer or can be caused by benign processes such as prostatitis. Endorectal coil MRI remains limited in its ability to identify microscopic or early macroscopic extraprostatic extension due to restrictions on spatial resolution and motion artifacts. In one study, MRI depicted only one of seven lesions with under 1 mm of ECE compared with five of seven with greater than 1 mm of ECE.

Early studies from the 1990s reported accuracies from 51% to 82% in distinguishing T2 and T3 disease. More recent reports on staging for organ-confined versus extracapsular disease have shown accuracies more consistent and relatively improved to around 90% accuracy. Also, erMRI has been shown to improve the prediction of neurovascular bundle invasion prior to radical prostatectomy.

Expertise with prostate MRI can improve staging accuracy. For example readers considered more "expert" in one case series were found to be more accurate in judging ECE compared with "nonexpert" readers and all other predictive variables. In another study, one more experienced reader achieved an accuracy of 91%, while the other had an accuracy of only 56%. A group of investigators demonstrated that the differences between "expert" readers and less experienced readers could be reduced by incorporating other clinical data (e.g., PSA value, tumor grade) and using strict imaging criteria.

Accurate stage assessment for individual lesions requires confident lesion detection. One study has shown that using DCE-MRI in conjunction with

T2-weighted images can improve staging performance by less experienced readers. Endorectal MRI has also been shown to be accurate in demonstrating SVI. The combination of a tumor at the base of the prostate that extends beyond the capsule and a low signal in the seminal vesicles (SVs) that have lost normal architecture is highly predictive of SVI.

Strategies that include erMRI of neural networks for staging have resulted in overall accuracies of 88% to 91% depending on implementation, which is better than the results obtained by using Partin tables. In this study Gleason score was found to be the most influential predictive factor, followed by erMRI results and PSA levels. Several studies have documented that erMRI is most successful in men with intermediate-risk prostate cancer based on Partin tables. In these men, erMRI staging was highly predictive of PSA recurrence. A study involving 344 patients demonstrated that erMRI added statistically meaningful staging data regarding ECE. Endorectal MRI has also proven helpful in directing 3D conformal radiotherapy and improving outcomes.

Magnetic Resonance Spectroscopy

One group of investigators demonstrated that prostate cancers have a characteristic loss of the citrate peak and gain in the choline/creatine peak on MRSI. Moreover, the ratio of choline to citrate is related to the Gleason score, suggesting that MRSI may provide information about tumor aggressiveness. Incremental improvement in accuracy of cancer detection and staging has been reported when MRSI was added to erMRI alone. As an indicator of outcome, MRSI has been shown predictive of biochemical recurrence. However, a recent American College of Radiology Imaging Network (ACRIN®) multicenter trial showed no incremental benefit of MR spectroscopy for localizing prostate cancer over 1.5T erMRI alone. Thus, MRSI cannot yet be considered to provide significant advantages in local staging prior to treatment.

Dynamic Contrast-enhanced Magnetic Resonance Imaging

Prostate cancers, like many tumors, demonstrate angiogenesis that can be detected on DCE-MRI. DCE-MRI demonstrates earlier and more intense enhancement in sites of tumor compared with the normal peripheral zone. One group of investigators found minimal improvements in diagnostic accuracy over conventional T2-weighted scans using DCE-MRI. Another group showed that tumors could be distinguished from noncancerous prostate with high reliability, although the study did not specifically address staging. Since accurate stage assignment requires tumor focus detection, it is felt that DCE-MRI can aid in confident localization of cancer foci, and thus DCE-MRI can improve staging performance when used in conjunction with T2-weighted images for less experienced readers when compared to more experienced readers. One study has demonstrated that the combination of high-spatial-resolution DCE-MRI and T2-weighted images improved assessment of ECE and yielded better results for prostate cancer staging compared with either technique independently. Other recent reports confirm the utility of DCE-MRI in cancer foci detection. However, this method still suffers from a lack of a uniformly accepted analytic method and has not been tested in multi-institutional trials. Thus, the benefit of DCE-MRI as a significant contributor to staging has not been established.

Diffusion-weighted Magnetic Resonance Imaging

The incorporation of DWI into MRI prostate imaging gives yet another method to improve prostate tumor detection and localization compared to T2-weighted images alone. It has shown some utility as a biomarker predictive of histologic grade. As with other parameters such as DCE-MRI, the incremental benefit in local staging in men with established prostate cancer has not been well established.

Multiparametric Magnetic Resonance Imaging of the Prostate

Multiparametric imaging with MRI refers to assessment using T2-weighted anatomical images combined with at least two other functional imaging methods (DCE-MRI, DWI, and MRSI). As outlined in descriptions thus far, MRI techniques are individually limited in accuracy for diagnosis and staging, but using them together yields greater accuracy. While it is premature to make specific recommendations as to guidelines for multiparametric assessments, expert international opinion is coalescing around this approach as representing the best available tool for imaging assessments in prostate cancer.

Nodal Staging with Magnetic Resonance Imaging

MRI has been shown to be at least equivalent to computed tomography (CT) for detecting abnormal LNs in men with prostate cancer. Unfortunately, metastatic LNs in prostate cancer are often small, so that conventional size criteria underestimate the extent of nodal disease. Thus, low sensitivities are observed, even in high-risk patients.

Computed Tomography

CT of the abdomen and pelvis suffers from poor sensitivity in detecting extraprostatic disease, including SVI and nodal involvement. CT should be reserved for use in patients with a higher probability of metastases. Overall accuracy in staging was reported as 65% by one study and 67% by another. For locoregional staging, such as extraprostatic extension, the accuracy has been reported as low as 24%. CT for lymph node staging in a contemporary population of surgical candidates has shown only 55% accuracy. The positive yield of CT for PSA values up to 20 ng/ml is less than

12%. Thus, it is generally felt that CT is of relatively low value in initial staging and in assessing the local extent of prostatic carcinoma in low- to intermediate-risk patients. The yield for CT of about 20% is more appropriate for advanced and high-risk disease, characterized by high PSA values >50 ng/ml or Gleason sum 8 or greater with PSA of at least 20 ng/ml. For these individuals, staging with CT of abdomen, pelvis, and sometimes chest may be used to establish the extent of disease, to determine fitness for localized treatment and for monitoring therapy.

Indium Capromab

The reliability and usefulness of indium-111 radiolabeled capromab pendetide (a first-generation monoclonal antibody against prostate-specific membrane antigen [PSMA]) scan as a method to stage prostate cancer remain unproven. Initial studies suggested that this technology may improve the detection of metastatic LNs. A group of researchers conducted histopathological correlation in LNs after In-111 scan in 31 patients (43 samples). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy value were 94%, 42%, 53%, 92%, and 65%, respectively. Its limitations appear to be due to the intracellular binding site of the antibody as well as nonprostatic expression of PSMA. In-111 scanning as an initial staging procedure is not recommended based on evidence at this time.

Bone Scan

The traditional modern bone scan for metastatic survey is performed with ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP). It is a standard component of the evaluation for many patients diagnosed with prostate cancer and can be performed with planar images or single-photon emission computed tomography (SPECT). Work by several researchers has shown that in patients with low PSA level (<10 ng/ml) who have no pain, the yield of a staging bone scan is too low to warrant its routine use. In their experience, no patient with a PSA ≤10 ng/ml had a positive bone scan, and only one patient in 300 with a PSA level ≤20 ng/ml had a positive radionuclide bone scan. Such observations have been confirmed by more recent studies as well. These studies suggest that for patients with no skeletal symptoms and a serum PSA level of ≤10 ng/ml, a staging radionuclide bone scan is not necessary; however, this recommendation has to be modified under specific circumstances such as T3 or T4 disease or a high Gleason score.

The rate of positive bone scans depends on the PSA value and Gleason score. Patients with PSA ≤20 ng/mL and Gleason Score <8 have a 1% to 13% rate of positive bone scans. For this reason only patients with a PSA ≥20 ng/mL (with any T stage or Gleason score), locally advanced disease (T3 or T4 with any PSA or Gleason score), or Gleason score ≥8 (with any PSA or T stage) should be considered for a radionuclide bone scan. Patients with skeletal symptoms or advanced stage disease should also be considered candidates for bone scans.

A growing alternative imaging test for diagnosing bone metastases is ^{18}F-fluoride positron emission tomography (PET), and ^{18}F-fluoride PET/CT. One study prospectively evaluated ^{18}F-fluoride PET, and ^{18}F-fluoride PET/CT against both planar and SPECT ^{99m}Tc-MDP bone scan and found that ^{18}F-fluoride PET/CT was the most accurate, followed by ^{18}F-fluoride PET alone, ^{99m}Tc-MDP SPECT and planar ^{99m}Tc-MDP. A 2010 meta-analysis solidifies superiority of ^{18}F-fluoride PET, and ^{18}F-fluoride PET/CT over MDP scans. The establishment of the NOPR (National Oncologic PET Registry), initially intended to assess PET using the most commonly available tracer, fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT in clinical practice, resulted in the Centers for Medicare and Medicaid Services (CMS) providing coverage for FDG-PET/CT for a wide variety of cancers. NOPR opened a registry in 2011 dedicated to ^{18}F-fluoride PET for bone metastases. Clinical evidence is accumulating at research centers, but as of this writing, results are not yet available, and CMS has not granted coverage at sites other than NOPR participant sites.

Positron Emission Tomography

The role of PET and PET/CT in the staging workup of newly diagnosed and recurrent prostate cancer is still being evaluated. It has the potential to play an important role in detecting early metastatic spread and monitoring post-therapy response. FDG-PET has proved disappointing in the initial staging of clinically localized prostate cancer. In that study, 23 of 24 primary prostate cancer lesions were not detected by FDG-PET. FDG-PET can play a role in the detection of local recurrence and/or distant metastases with increasing PSA after initial treatment failure. Several additional radiotracers have been extensively studied, including C11 or F18 choline and acetate, C11 methionine, ^{18}F-fluoride, gallium-68–labeled peptides, and fluorodihydrotestosterone. These radiotracers can have advantages over traditional agents, and their use may help in the clinical decision-making process, especially in patients with high-risk primary disease. For instance, the use of C11 choline or acetate PET appears to be promising for detecting nodal metastases. But such agents remain limited in availability, so PET scanning has a limited role in the staging of prostate cancer at present.

Radiography

There are no data in the literature documenting the yield of a chest radiograph. Therefore, it should be performed as part of the initial staging only with suspected metastatic disease (e.g., PSA >100 ng/mL) or in patients who are heavy smokers with clinically localized disease.

In addition, radiographs can be useful in the evaluation of bone pain, or workup of bone scan findings. Any part of the body might be imaged based on suspicion, especially those in the proximal appendicular skeleton when falling outside the coverage of a CT or MRI examination (if performed).

Active Surveillance and the Role of Imaging

The concept of active surveillance stems from the fact that there is great variability in outcomes among men diagnosed with low-risk stratified prostate cancer. In order to avoid overtreatment in cancers that would otherwise prove indolent or lacking aggressiveness, patients can undergo a period of active surveillance (sometimes called watchful waiting) consisting of deferred treatment along with disease monitoring, usually with PSA, DRE, and sometimes repeat biopsy. The rationale is to allow some time to discover the natural history of disease and so determine if therapies, with associated treatment risks, are worth implementing. Approximately 30% (14% to 41%) of patients who are initially found to be appropriate for active surveillance will progress to active treatment after intermediate follow-up (radical prostatectomy or radiation).

Imaging with MRI has been studied and advocated as an aid in this process, especially to detect cases that have been understaged and misclassified. Some patients after imaging can undergo rebiopsy directed to MRI-suspected cancer sites and be reclassified as having higher risk features and deserving therapy. However, the absence of disease on MRI may be less helpful; a retrospective assessment found that MRI with MRSI that was negative for cancer foci in men undergoing active surveillance was not an accurate predictor of biochemical outcomes. Active surveillance as an approach is still somewhat controversial and under evaluation to determine if those men with more aggressive cancers are at higher risk for treatment failure after the delay in treatment initiation.

Summary

- Pretreatment staging of prostate cancer should be individualized based on consideration of the clinical parameters that are predictive of the likelihood of extraprostatic extension, SVI, and metastatic disease. These clinical parameters can include the pretreatment PSA level and the rate of rise or doubling time, the Gleason score, the T stage from DRE, and sometimes the number of positive biopsies, including percentage of the core involved.
- Imaging in low-risk patients is likely to have a low yield in providing useful information to guide management for those electing up-front treatment. There may be a role for MRI in the context of active surveillance for low-risk patients.
- In intermediate-risk and high-risk individuals, imaging has a role in staging and in selecting or tailoring therapy. MRI appears to be the most accurate imaging test available for local staging of the prostate, providing both locoregional and nodal evaluation. Use of endorectal coil at 1.5 T is recommended, and at 3.0 T is preferred. The accuracy of the technique appears related to the experience of the radiologists. MRSI, DCE-MRI, and DWI-MRI appear to be useful adjuncts, but incremental benefits provided by these additional MRI techniques over T2-weighted imaging for staging remain unproven in multi-institutional trials. Consensus is building around multiparametric prostate MRI as the most accurate and useful approach.
- In patients with the high-risk disease (clinical T3, very high PSA levels, and Gleason score ≥8), radionuclide bone scans and CT can be useful for detecting metastases. PET scans with FDG are of limited value in initial staging.
- When there exists strong clinical suspicion for the presence of prostate cancer in an individual due to rising or persistent high PSA despite (generally multiple) negative biopsy sessions, MRI may be useful in identifying cancer in the prostate that can be targeted for diagnosis.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 m^2), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 m^2. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Abbreviations

- AJCC, American Joint Committee on Cancer
- CT, computed tomography
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography
- In, indium
- MRI, magnetic resonance imaging

- PSA, prostate-specific antigen
- T, tumor
- Tc, technetium

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Prostate cancer

Guideline Category

Evaluation

Risk Assessment

Screening

Clinical Specialty

Internal Medicine

Nuclear Medicine

Oncology

Radiology

Urology

Intended Users

Health Plans

Hospitals

Managed Care Organizations

Physicians

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of initial radiologic examinations for pretreatment detection, staging, and surveillance of patients with prostate cancer

Target Population

Patients with prostate cancer

Interventions and Practices Considered

1. X-ray area of interest
2. Computed tomography (CT) abdomen and pelvis
    - With contrast
    - Without contrast
    - Without and with contrast
3. Magnetic resonance imaging (MRI) pelvis
    - Without and with contrast
    - Without contrast
4. Technetium (Tc)-99m bone scan whole body
5. Fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET)/CT whole body
6. Indium (In)-111 capromab pendetide scan

Major Outcomes Considered

Accuracy, sensitivity, specificity, and positive and negative predictive value of radiologic procedures for pretreatment staging of prostate cancer

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Procedure

The Medline literature search is based on keywords provided by the topic author. The two general classes of keywords are those related to the condition (e.g., ankle pain, fever) and those that describe the diagnostic or therapeutic intervention of interest (e.g., mammography, MRI).

The search terms and parameters are manipulated to produce the most relevant, current evidence to address the American College of Radiology Appropriateness Criteria (ACR AC) topic being reviewed or developed. Combining the clinical conditions and diagnostic modalities or therapeutic procedures narrows the search to be relevant to the topic. Exploding the term "diagnostic imaging" captures relevant results for diagnostic topics.

The following criteria/limits are used in the searches:

1. Articles that have abstracts available and are concerned with humans.
2. Restrict the search to the year prior to the last topic update or in some cases the author of the topic may specify which year range to use in the search. For new topics, the year range is restricted to the last 5 years unless the topic author provides other instructions.
3. May restrict the search to Adults only or Pediatrics only.
4. Articles consisting of only summaries or case reports are often excluded from final results.

The search strategy may be revised to improve the output as needed.

Number of Source Documents

The total number of source documents identified as the result of the literature search is not known.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Strength of Evidence Key

Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis, and results.

Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.

Category 3 - The conclusions of the study may be valid, but the evidence supporting the conclusions is inconclusive or equivocal.

Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author drafts or revises the narrative text summarizing the evidence found in the literature. American College of Radiology (ACR) staff draft an evidence table based on the analysis of the selected literature. These tables rate the strength of the evidence for all articles included in the narrative text.

The expert panel reviews the narrative text, evidence table, and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the table. Each individual panel member forms his/her own opinion based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Modified Delphi Technique

The appropriateness ratings for each of the procedures included in the Appropriateness Criteria topics are determined using a modified Delphi methodology. A series of surveys are conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. American College of Radiology (ACR) staff distributes surveys to the panelists along with the evidence table and narrative. Each panelist interprets the available evidence and rates each procedure. The surveys are completed by panelists without consulting other panelists. The ratings are a scale between 1 and 9, which is further divided into three categories: 1, 2, or 3 is defined as "usually not appropriate"; 4, 5, or 6 is defined as "may be appropriate"; and 7, 8, or 9 is defined as "usually appropriate." Each panel member assigns one rating for each procedure per survey round. The surveys are collected and the results are tabulated, de-identified and redistributed after each round. A maximum of three rounds are conducted. The modified Delphi technique enables each panelist to express individual interpretations of the evidence and his or her expert opinion without excessive bias from fellow panelists in a simple, standardized and economical process.

Consensus among the panel members must be achieved to determine the final rating for each procedure. Consensus is defined as eighty percent (80%) agreement within a rating category. The final rating is determined by the median of all the ratings once consensus has been reached. Up to three rating rounds are conducted to achieve consensus.

If consensus is not reached, the panel is convened by conference call. The strengths and weaknesses of each imaging procedure that has not reached consensus are discussed and a final rating is proposed. If the panelists on the call agree, the rating is accepted as the panel's consensus. The document is circulated to all the panelists to make the final determination. If consensus cannot be reached on the call or when the document is circulated, "No consensus" appears in the rating column and the reasons for this decision are added to the comment sections.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current literature and expert panel consensus.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Selection of appropriate radiologic imaging procedures for pretreatment detection, staging, and surveillance of patients with prostate cancer

Potential Harms

Gadolinium-based Contrast Agents

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (i.e., <30 mL/min/1.73 m^2), and almost never in other patients. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73 m^2. For more information, please see the American College of Radiology (ACR) Manual on Contrast Media (see the "Availability of Companion Documents" field).

Relative Radiation Level (RRL)

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

The American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Eberhardt SC, Carter S, Casalino DD, Merrick G, Frank SJ, Gottschalk AR, Leyendecker JR, Nguyen PL, Oto A, Porter C, Remer EM, Rosenthal SA, Expert Panels on Urologic Imaging and Radiation Oncology-Prostate. ACR Appropriateness CriteriaÂ® prostate cancer -- pretreatment detection, staging, and surveillance. [online publication]. Reston (VA): American College of Radiology (ACR); 2012. 12 p. [119 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2005 (revised 2012)

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panels on Urologic Imaging and Radiation Oncology–Prostate

Composition of Group That Authored the Guideline

Panel Members: Steven C. Eberhardt, MD (*Principal Author*); Scott Carter, MD (*Research Author*); David D. Casalino, MD (*Co-Chair*); Gregory Merrick, MD (*Co-Chair*); Steven J. Frank, MD; Alexander R. Gottschalk, MD, PhD; John R. Leyendecker, MD; Paul L. Nguyen, MD; Aytekin Oto, MD; Christopher Porter, MD; Erick M. Remer, MD; Seth A. Rosenthal, MD

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

Guideline Availability

The updated guideline is available from the American College of Radiology (ACR) Web site .

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

Availability of Companion Documents

The following are available:

- ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2 p. Available from the American College of Radiology (ACR) Web site .
- ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 1 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Evidence table development – diagnostic studies. Reston (VA): American College of Radiology; 2013 Nov. 3 p. : Available from the ACR Web site .
- ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2 p. : Available from the ACR Web site .
- ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 90 p. Available from the ACR Web site .
- ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 1 p. Available from the ACR Web site .
- ACR Appropriateness Criteria® prostate cancer—pretreatment detection, staging and surveillance. Evidence table. Reston (VA): American College of Radiology; 2012. 45 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on November 15, 2004. The information was verified by the guideline developer on December 21, 2004. This summary was updated by ECRI on March 23, 2006, December 4, 2007, and on June 17, 2010. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on May 9, 2013.

Copyright Statement

Disclaimer

NGC Disclaimer

The National Guideline Clearinghouseâ„¢ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.